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April 5/95

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Attention: Dr. Luc Montagnier

Dear Dr. Montagnier,

I was very pleased to read your abstract from the IUVDT in Singapore, and to hear your presentation. My free paper is on page 45 of the Congress abstracts.

I note that you say "silent bacterial or viral infections" may contribute to the oxidative stress and viral and immune system activation. Almost all human and experimental subjects who are infected with *T.pallidum* a second time have no immunologic memory unless the first exposure was treated curatively. The concept of silent syphilis is an old one, dating from the 1920s. I feel that we need to address the immunoregulation responsible for the non-anamnestic state. I think that syphilis presents a double cytokine hazard to its hosts. Firstly there is the concept of immunodeviation (Th-2 predominance) that has appeared in the syphilis literature termed as "split tolerance" and was recently reviewed by Stewart Sell in IMMUNOLOGY TODAY, December, 1993. Secondly, there is the question of tissue injury (the non-specific response to *T.pallidum*) and the repair regulation cytokine TGF-beta. For a review of the very potent CD4 modulation of this cytokine, you could read Wadhwa's paper in BLOOD, Sept 15, 1994. The control of the TGF-beta contamination in factor replacement for haemophilia is the first successful AIDS treatment intervention I have seen, and hopefully it will continue to work. We have never pinned down the so-called "serum factors" that were the subject of much work with syphilitic sera and its in-vitro cell regulation. If you wished to read about the pre-AIDS and pre-1983 understanding of the immunoregulatory effects of syphilis, Dekker's IMMUNOLOGY SERIES 20 is devoted to the treponematoses.

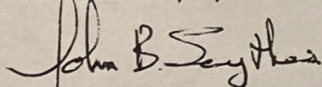
Three years ago I spoke briefly with Michel Poitevin and Jean-Michel Alonso at your Institut Fournier. At that time, my understanding of cytokines and their possible role in infectious disease pathogenesis was limited. Only recently have some centres

identified what is going on at this level in those who develop chronic bacterial diseases. I think the response in human treponematoses is very similar to the response to the Chagas trypanosome and the kala-azar Leishmaniasis, in that there is a great polarity. Do you think that powerful effector cell downmodulators such as IL-10 and TGF-beta could suppress CD4 maturation or injure the phenotype in such a way that it programs the cell for apoptoses? It seems to me that these very cytokines must operate in syphilis to explain the experimental and human immunologic memory defect that sets in after a few months of natural and untreated infection.

If all this interested you more, I would very much appreciate an opportunity to discuss it further. I will be in Europe for the first two weeks of July, and as well, I hope to attend the ISSTR in New Orleans.

I look forward to hearing from you.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "John B. Scythes". The signature is fluid and cursive, with the first name "John" and last name "Scythes" clearly distinguishable.

John B. Scythes
JBS/klm